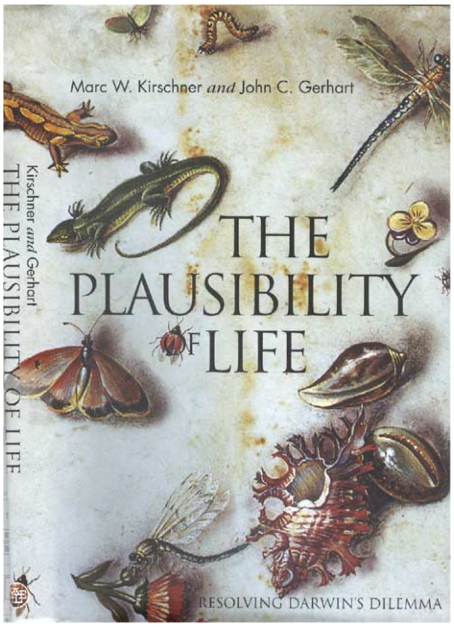
Cell, Vol. 123, 177–179, October 21, 2005, Copyright ©2005 by Elsevier Inc. DOI 10.1016/j.cell.2005.10.003

Book Review

A Variable Look at Evolution

The Plausibility of Life
By Marc W. Kirschner and John C. Gerhart
New Haven, CT: Yale University Press (2005). 336 pp. $30.



The diversity and complexity of life on Earth—from bacteria and fungi to plants and animals—suggest the generation of remarkable variation upon which natural selection can act. But how do new traits—new morphological architectures (bodyplans), developmental processes, and behaviors—arise? Did the vertebrate brain and neural crest arise through processes that are different from those that generated new hairs on the legs of the fruit fly? Can major evolutionary transitions in the history of life be explained by random variation—variation that is random with respect to the future needs of the organism—filtered through the process of natural selection? These questions are not new, but the promise of a more mechanistic basis for answering them through comparative developmental biology imbues them with a fresh urgency.

The origin of new phenotypes (that is, phenotypic novelty) during evolution is the subject of a new book, *The Plausibility of Life*, by Marc Kirschner of Harvard Medical School and John Gerhart of the University of California, Berkeley. In this book, the authors significantly extend their earlier work on the ability of organisms to evolve (evolvability), culminating in their theory of "facilitated variation." In their earlier work on evolvability, Kirschner and Gerhart argued that many aspects of gene regulation and development have had the effect of enhancing the evolutionary adaptability of species and lineages. For example, phenotypic plasticity (that is, the production of different phenotypes under various environmental conditions) allows a species to inhabit a wider range of environments. Their new book expands upon this argument, suggesting that animals have evolved a number of factors in addition to genetic mutation that combine "to determine the nature and degree of variation, thus giving selection more abundant viable variation on which to act." In Kirschner and Gerhart's view, there are four aspects of gene regulation and development in animals that constrain the direction of heritable variation. These are the extensive conservation across metazoa of certain regulatory patterns; a modular pattern of organismal design; what the authors term "weak linkages" in gene regulation, caused by, in their view, regulatory interactions that do not specify outcomes; and nondeterministic outcomes of development.

In the old debate between the primacy of genetic mutation versus natural selection as the force that drives phenotypic change, Kirschner and Gerhart clearly feel that natural selection needs some help. That help comes, they suggest, in the form of random genetic variation that is biased toward viability, functional utility, and relevance to environmental conditions. This is the first place where the authors get into trouble; for through much of the book they seem to fundamentally misunderstand how evolutionary biologists use the term "random." By random mutation, evolutionary biologists mean random with respect to the adaptive needs of the organism, not, as the authors would have it in the early part of the book, completely random in the sense that many nonevolutionary biologists may think of the word "random." One of Charles Darwin's key insights was that the combination of undirected mutation and natural selection is a powerful positive force for evolutionary creativity (and not, as so many later biologists have suggested, merely a negative force). Evolutionary biologists have long understood that the nature of variation depends critically on what has already evolved. Indeed, there is a rich literature discussing how phylogeny, function, structure, and other features constrain evolutionary variation. Kirschner and Gerhart ignore this uncomfortable fact, dismissing constraint as "a minor effect, or trivial, for example, in explaining why mollusks (sic) and echinoderms were less able to evolve wings than vertebrates." They refer to variation as random alterations that can have little positive impact or that "lead to catastrophic failure." This results in the appearance of some odd comments as, for example, when the authors claim that evolutionary biologists "do not commonly appreciate…" that "present-day organisms come from previous organisms." Indeed. I would be more than happy to introduce Kirschner and Gerhart to some of their colleagues at Harvard and Berkeley who in fact spend much of their professional time addressing just this issue. I have belabored this point only because the authors' limited view of the evolutionary literature on variation and constraint undercuts most of their own arguments in favor of their theory of facilitated variation.

Kirschner and Gerhart's book must be placed in the context of a number of other recent contributions to evolutionary thought, all of which argue that the current model of evolution is incomplete. Although most of the other book authors have had the good grace (and good sense) not to proclaim in the preface that they are "propose[ing] a major new scientific theory…" and "an original, far-reaching recasting of evolutionary theory…," they do suggest some important extensions and modifications regarding the origin and establishment of phenotypic variation. Carl Schlichting and Massimo Pigliucci revitalized the concept of developmental reaction norms in their book *Phenotypic Evolution* (Sinauer, 1998), which integrates development, genetics, and environment. In her book, *Developmental Plasticity and Evolution* (Oxford University Press, 2003), Mary-Jane West-Eberhard extends the discussion of Schlichting and Pigliucci with an exhaustive focus on the importance of behavioral shifts and phenotypic plasticity in facilitating the establishment of evolutionary novelty. Eva Jablonka and Marion Lamb continue their explorations of the importance of epigenetics in their book *Evolution in Four Dimensions* (Bradford, 2005). The four dimensions of the title are the four sources of inheritance: genetics, epigenetics (for example, methylation, RNA interference), behavioral inheritance, and social learning (which in humans involves language and often writing and thus is considered symbolic inheritance). In different ways, each of these books suggests that patterns of variation are nonrandom. Further, these books imply that these biases in variation solve problems of evolutionary innovation that remain unresolved by the Modern Synthesis, the reigning paradigm of evolution developed in the 1940s by Mayr, Simpson, Wright, Haldane, Dozhansky, Fischer, and others. Kirschner and Gerhart build upon these previous revisionary treatments of evolution, usefully focusing on the role of gene regulation and development in constraining patterns of variation. Before turning to the question of whether all of these new books add up to a revision of the Modern Synthesis, it is worth considering the arguments of Kirschner and Gerhart in more detail.

The breadth of constraint among the genetic and developmental processes of metazoans has surprised many, if not most, developmental biologists. Kirschner and Gerhart invoke these conserved core processes as a critical element in the regulation of the types of variation that arise. They suggest that these core processes arose in waves of innovation associated with the first bacteria, early eukaryotes, multicellular organisms, the origin of metazoan, and a few other events. Presenting no evidence, they claim that these waves of innovation are not linked to changes in the physical environment. In fact, one of the most exciting areas of current research addresses how the origin and spread of these innovations *are* linked to a variety of geochemical, climatic, and other changes. These core processes—DNA, RNA, and protein synthesis, formation of the cytoskeleton, and limb patterning—have descended relatively unchanged since they first arose. Kirschner and Gerhart suggest that most evolution within the Animal Kingdom since the Cambrian radiation of metazoans involved the carefully regulated deployment of these core processes, and in this I think they are largely correct. As West-Eberhard describes in her book, physiological adaptations to new environmental conditions followed by stabilization of these features can be a rich source of new phenotypes. Kirschner and Gerhart propose that these new phenotypes are likely to be developmentally integrated and viable.

Three key architectural features of these core processes enable them to be linked in different ways to generate new phenotypes. The first is "weak linkage," that is, the nonspecific information contained in signal transduction and transcription pathways. By this, the authors mean that the signal merely triggers a response but does not contain information about what that response should be. The second is exploratory behavior, a form of somatic mutation that allows a wide variety of physiological responses to particular conditions, followed by evolutionary stabilization of the most useful. Kirschner and Gerhart invoke exploratory behavior as a means of avoiding what they view as an otherwise insurmountable difficulty: that novelty appears to require multiple, correlated changes from phenotype to function. The third key feature is compartmentalization of function, which is best exemplified by arthropods (although it is present in many other metazoans). The authors describe the developmental compartments of arthropods with the wonderful and most appropriate descriptor "invisible anatomy." The most important part of this book is, in my view, the authors' description of the evolutionary significance of the interactions between compartments and the conserved regulatory networks that underlie them via weak linkages. Although the authors do not emphasize this sufficiently (at least for a paleontologist), this network of relationships imposes a developmental reality to the architectural forms described as body plans and generally characterized within Linnean systematics as phyla and classes. As Kirschner and Gerhart note, this modularity of design often allows relatively independent evolution of different body parts without greatly increasing the coordination among them. The gills, paddles, mouthparts, claws, and walking legs of various arthropods are all modifications of a single ancestral structure. The modularity of arthropod body plans has enabled the rapid adaptation of limbs without inhibiting the workings of the whole animal.

Kirschner and Gerhart have tackled one of the most challenging issues in evolution, and many parts of this book provide insightful new ways of approaching the issue of phenotypic novelty. They have not set out to provide a complete account of the origin of novelty but rather have attempted to address one of the critical aspects of any such account: the initial generation of variation. Given the expressed ambitions of the authors for the book, there are aspects of their narrative that are troubling. Although, laudably, Kirschner and Gerhart wrote the text at a fairly general level to attract both a wide range of biologists as well as scientifically literate members of the general public, this is a risky strategy when claiming a major theoretical advance. The lack of justification and depth in the detail and the often dated or scanty references leave far too much to the imagination of the reader. Ultimately, their contribution feels more like a vision of where the field should go rather than a thoroughly constructed theory of the origins of phenotypic novelty.

Stephen Jay Gould's modestly entitled opus *The Structure of Evolutionary Theory* (Harvard University Press, 2002) presents yet another thread in the modification of the Modern Synthesis. Gould's book provides an extensive survey of the development of evolutionary theory. It also presents a detailed defense of a hierarchical expansion of evolution with selection on multiple levels: not just selection among individuals within a population but also among different cell types, species, and even clades. Here, phenotypic novelty is not so much an issue of the generation and establishment of variation as it is the differential success of some species and lineages. What is striking about these recent books that air revisionist views of evolution (except that of West-Eberhard) is that they fail to adequately address the success of phenotypic novelty. Kirschner and Gerhart are to be congratulated for tackling this issue in a forthright fashion. The generation of morphological variants is a critical issue, and several of these book authors have raised important questions and proposed new viewpoints. But the generation of variation is only the beginning of the problem of evolutionary novelty. Novel phenotypes succeed or fail based on their ecological relationships with other organisms and with the physical environment. This ecological dimension is conspicuously lacking in these books, yet we cannot really understand novelty without it. In particular, evolutionary biologists need to address such issues as how phenotypic "space" expands, how new niches are constructed, and related ecological events.

Is the neo-Darwinian view of evolution in need of reformation? Certainly the diversity of rumblings indicates some degree of unhappiness, but evolutionary biologists have regularly published new models of evolution since the late 19th century (see Bowler, *The Eclipse of Darwinism*, Johns Hopkins, 1993). Is there reason to think that our view of evolution needs to change? The answer is almost certainly yes, although not, as the purveyors of creationism/intelligent design would have it, because the reality of evolution is under question. Rather, we need to revise our view of evolution to reflect a more detailed understanding of how genetics and development both allow and facilitate phenotypic variation, to take into account the temporal dynamics of changes in the environment, and to incorporate the likelihood that there is selection and feedback at multiple levels (cell, tissue, organism, clade). The central issues that need to be incorporated into evolutionary theory are the origin of phenotypic novelty and the discontinuous patterns of appearance of new phenotypes. *The Plausibility of Life* is a fairly light and even entertaining read, as long as it is taken as a general introduction to recent ideas in evolution and comparative developmental evolution, many of which have emerged from the incredible discoveries of the past few years. But with its sometimes troubling limitations, the book falls short of the major new theory that the authors promise in their introduction.

Douglas H. Erwin[1,2]
[1]Department of Paleobiology, MRC-121
National Museum of Natural History
Washington D.C. 20013
[2]Santa Fe Institute
1399 Hyde Park Road
Santa Fe, New Mexico 87501